

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Maria Adele Pacciarini et al. **Examiner:** Ganapathy Krishnan
Serial No.: 09/786,998 **Art Unit:** 1623
Filed: June 14, 2001 **Docket:** 17815
For: USE OF METHOXYMORPHOLINO DOXORUBICIN FOR THE TREATMENT OF A LIVER TUMOR **Dated:** November 7, 2011

Confirmation No.: 1122

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

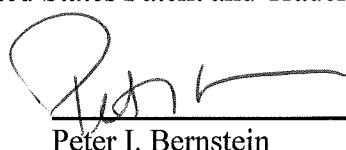
In accordance with 37 C.F.R §§1.97 and 1.98, it is requested that the following references, which are also listed on the attached Information Disclosure Citation, be made of record in the above-identified case.

1. De Takats P.G. et al., "Phase IB Study of Methoxymorpholinodoxorubicin (PNU152243; FCE 23762) Administered in a 3 or 4 Weekly Schedule", *Clinical Pharmacology and Phase I Studies* (September 18, 1997), Abstract;
2. Quintieri L. et al., "Delivery of Methoxymorpholiny Doxorubicin by Interleukin 2-Activated NK Cells: Effect in Mice Bearing Hepatic Metastases", *British Journal of Cancer* 79(7/8):1067-1073 (March 1999);

CERTIFICATE OF ELECTRONIC FILING

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Dated: November 7, 2011



Peter I. Bernstein

3. Vasey P.A. et al., "Phase I Clinical and Pharmacokinetic Study of 3'-Deamino-3'-(2-Methoxy-4-Morpholinyl)Doxorubicin (FCE 23762)", *Cancer Research* 55(10):2090-2096 (May 15, 1995);
4. Taub R.N. et al., "Phase II Study of Methoxymorpholinodoxorubicin in Advanced Sarcomas (PNU/S2243 (FCE 23762))", *Proceedings of the Annual Meeting of the America Society of Clinical Oncology Vol. 16* (May 17-20, 1997), Abstract;
5. Robert J. et al., "Pharmacokinetics and Metabolism of Anthracyclines", *Cancer Surveys* 17:219-252 (1993);
6. Rougier P. et al., "Intérêt Des Chimiothérapies Loco-Régionales Par Les Anthracyclines", *Pathologies Biologie* 35(1):123-128 (1987);
7. Kirk S. et al., "Irresectable Hepatoma Treated by Intrahepatic Iodized Oil Doxorubicin Hydrochloride: Initial Results", *Surgery* 109(6):694-697 (1991);
8. Carr B.I. et al., "Prolonged Survival With Chemotherapy Alone for Hepatocellular Carcinoma (HCC) With Intra-Arterial Chemotherapy" *Proceedings of the American Society of Clinical Oncology Vol. 13* (March 1994), Abstract;
9. Carr B.I. et al., "Phase II Study of Spherex (Degradable Starch Microspheres) Injected into the Hepatic Artery in Conjunction With Doxorubicin and Cisplatin in the Treatment of Advanced-Stage Hepaocellular Carcinoma: Interim Analysis", *Seminars in Oncology* 24(2), Suppl 6 pp. S6-97-S6-99 (April 1997);
10. Lai E.C.S., "Postoperative Adjuvant Chemotherapy After Curative Resection of Hepatocellular Carcinoma: A Randomized Controlled Trial", *Arch. Surg.* 133:183-188 (February 1998);
11. Ripamonti M. et al., "In Vivo Anti-Tumour Activity of FCE 23762, a Methoxymorpholinyl Derivative of Doxorubicin Active on Doxorubicin-Resistant Tumour Cells", *Br. J. Cancer* 65:703-707 (1992);
12. Ripamonti M. et al., "Morpholinylanthracyclines: Cytotoxicity and Antitumor Activity of Differently Modified Derivatives", *Investigational New Drugs* 14:139-146 (1996);
13. Capranico G. et al., "Influence of Structural Modifications at the 3' and 4' Positions of Doxorubicin on the Drug Ability to Trap Topoisomerase II and to Overcome Multidrug Resistance", *Molecular Pharmacology* 45:908-915 (1994);

14. Winette T.A. et al., "The Role of Methoxymorpholino Anthracycline and Cyanomorpholino Anthracycline in a Sensitive Small-Cell Lung-Cancer Cell Line and its Multidrug-Resistant but P-Glycoprotein-Negative and Cisplatin-Resistant Counterparts", *Cancer Chemother Pharmacol.* 35:345-348 (1995);
15. Duran G.E. et al., "Differential Single-Versus Double-Strand DNA Breakage Produced by Doxorubicin and its Morpholiny Analogues", *Cancer Chemother Pharmacol.* 38:210-216 (1996);
16. Geroni C. et al., "L1210 Cells Selected for Resistance to Methoxymorpholiny Doxorubicin Appear Specifically Resistant to this Class of Morpholiny Derivatives", *Br. J. Cancer* 69:315-319 (1994);
17. Bakker M. et al., "Mechanisms for High Methoxymorpholino Doxorubicin Cytotoxicity in Doxorubicin-Resistant Tumor Cell Lines", *Int. J. Cancer* 73:362-366 (1997);
18. Bielack S.S. et al., "Structurally Modified Anthracyclines Retain Activity in a Cell Line With Simultaneous Typical and Atypical Multidrug Resistance", *Anticancer Research* 15:1279-1284 (1995);
19. Colleoni et al., "Arterial Chemoembolization With Epirubicin in Unresectable Hepatocellular Carcinoma in Cirrhosis", *Ann. Oncol. Vol. 5(Suppl 8)* (1994), Abstract;
20. Lai C.L. et al., "Doxorubicin Versus No Antitumor Therapy in Inoperable Hepatocellular Carcinoma. A Prospective Randomized Trial", *Cancer Vol. 62(3)*:479-483 (August 1, 1988), Abstract;
21. Shepherd FA et al., "Treatment of Primary Hepatocellular Carcinoma by Hepatic Arterial Infusion of 4'-Epirubicin (Eng.)", *Reg Cancer Treat Vol. 3(4)*:197-201 (1990), Abstract;
22. Ono T. et al., "Adjuvant Chemotherapy With Epirubicin and Carmofur After Radical Resection of Hepatocellular Carcinoma: A Prospective Randomized Study", *Semin Oncol. Vol. 24(2 Suppl 6)*:S6-18-S6-25 (April 1997), Abstract;
23. Wassermann K. et al., "Effects of Morpholiny Doxorubicins, Doxorubicin, and Actinomycin D on Mammalian DNA Topoisomerases I and II", *Mol. Pharmacol.* 38(1):38-45 (July 1, 1990), Abstract;
24. Takayasu Y. et al., "Merits and Demerits of Arterially Administered Large-Dose Anticancer Agent, Lipiodol Emulsion", *Cancer and Chemotherapy* 15(8-Part-II):2562-2567 (1988);

25. English-language machine translation of Russian Patent Application No. RU 2 065 307, published August 20, 1996; and

26. International Search Report dated May 3, 2000 received from the European Patent Office from related International Patent Application No. PCT/EP99/06298.

Applicants are submitting a copy of the above-cited references required by 37 C.F.R. § 1.98 (a)(2)(i) and (ii), together with a copy of the International Search Report.

Inasmuch as this Information Disclosure Statement is being submitted in accordance with the schedule set out in 37 C.F.R. §1.97(c), please charge the \$180.00 fee to deposit account no. 19-1013/SSMP.

Respectfully submitted,



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(Use several sheets if necessary)		Applicants Maria Adele Pacciarini et al.	
		Filing Date June 14, 2001	Group Art Unit 1623
OTHER (Including Author, Title, Date, Pertinent Pages, Etc.)			
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EXAMINER	/Ganapathy Krishnan/	DATE CONSIDERED	12/30/2011

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